

FIG. 1 Sequence of CDRs of hTNF40

H1 DYGMN (SEQ ID NO:1)

H2 WINTYIGEPIYVDDFKG (SEQ ID NO:7)

H2' WINTYIGEPIYADSVKG (SEQ ID NO:2)

H3 GYRSYAMDY (SEQ ID NO:3)

L1 KASQNVGTNVA (SEQ ID NO:4)

L2 SASFLYS (SEQ ID NO:5)

L3 QQYNIYPLT (SEQ ID NO:6)

FIG.2 Murine VI Sequence of hTNF40 (SEQ ID NO: 99)

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10      20      30      40      50
GAC ATT GTG ATG ACC CAG TCT CAA AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG
CTG TAA CAC TAC TGG GTC AGA GTT TTT AAG TAC AGG TGT AGT CAT CCT CTG TCC
D   I   V   M   T   Q   S   Q   K   F   M   S   T   S   V   G   D   R>

60      70      80      90      100
GTC AGC GTC ACC TGC AAG GCC AGT CAG AAT GTG GGT ACT AAT GTA GCC TGG TAT
CAG TCG CAG TGG ACG TTC CCG TCA GTC TTA CAC CCA TGA TTA CAT CCG ACC ATA
V   S   V   T   C   K   A   S   Q   N   V   G   T   N   V   A   W   Y>

110     120     130     140     150     160
CAA CAG AAA CCA GGA CAA TCT CCT CCA AAA GCA CTG ATT TAC TCG GCA TCC TTC CTA
GTT GTC TTT GGT CCT GGT AGA GGA TTT CGT GAC TAA ATG AGC CGT AGG AAG GAT
Q   Q   K   P   G   Q   S   S   P   K   A   L   I   Y   S   A   S   F   L>

170     180     190     200     210
TAT AGT GGA GTC CCT TAT CGC TTC ACA GGC AGT GGA TCT GGG ACA GAT TTC ACT
ATA TCA CCT CAG GGA ATA GCG AAG TGT CCG TCA CCT AGA CCC TGT CTA AAG TGA
Y   S   G   V   P   Y   R   F   T   G   S   G   S   G   T   D   F   T>

220     230     240     250     260     270
CTC ACC ATC AGC ACT GTG CAG TCT GAA GAC TTG GCA GAG TAT TTC TGT CAG CAA
GAG TGG TAG TCG TGA CAC GTC AGA CTT CTG AAC CGT CTC ATA AAG ACA GTC GTT
L   T   I   S   T   V   Q   S   E   D   L   A   E   Y   F   C   Q   Q>

280     290     300     310     320
TAT AAC ATC TAT CCT CTC ACG TTC GGT GGT GGC ACC AAG CTG GAG CTG AAA CGT
ATA TTG TAG ATA GGA GAG TGC AAG CCA CGA CCC TGG TTC GAC CTC GAC TTT GCA
Y   N   I   Y   P   L   T   F   G   A   G   G   T   K   L   E   L   K   R>

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FIG.3 Murine Vh Sequence of hTNF40 (SEQ ID NO: 100)

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10      20      30      40      50
CAG ATC CAG TTG GTG CAG TCT GGA CCT GAG CTG AAG AAG CCT GGA GAG ACA GTC
GTC TAG GTC AAC CAC GTC AGA CCT GGA CTC GAC TTC TTC GGA CCT CTC TGT CAG
Q I Q L V Q S G P E L K K P G E T V>

60      70      80      90      100
AAG ATC TCC TGC AAG GCT TCT GGA TAT GTT TTC ACA GAC TAT GGA ATG AAT TGG
TTC TAG AGG ACG TTC CGA AGA CCT ATA CAA AAG TGT CTG ATA CCT TAC TTA ACC
K I S C K A S G Y V F T D Y G M N W>

110     120     130     140     150     160
GTG AAG CAG GCT CCA GGA AAG GCT TTC AAG TGG ATG GGC TGG ATA AAC ACC TAC
CAC TTC GTC CGA GGT CCT TTC CGA AAG TTC ACC TAC CCG ACC TAT TTG TGG ATG
V K Q A P G K A F K W M G W I N T Y>

170     180     190     200     210
ATT GGA GAG CCA ATA TAT GTT GAT GAC TTC AAG GGA CGA TTT GCC TTC TCT TTG
TAA CCT CTC GGT TAT ATA CAA CTA CTG AAG TTC CCT GCT AAA CGG AAG AGA AAC
I G E P I Y V D D F K G R F A F S L>

220     230     240     250     260     270
GAA ACC TCT GCC AGC ACT GCC TTT TTG CAG ATC AAC AAC CTC AAA AAT GAG GAC
CTT TGG AGA CGG TCG TGA CGG AAA AAC AAC GTC TAG TTG TTG GAG TTT TTA CTC CTG
E T S A S T A F L Q I N N L K N E D>

280     290     300     310     320
ACG GCT ACA TAT TTC TGT GCA AGA GGT TAC CGG TCC TAT GCT ATG GAC TAC TGG
TGC CGA TGT ATA AAG ACA CGT TCT CCA ATG GGC AGG ATA CGA TAC CTG ATG ACC
T A T Y F C A R G Y R S Y A M D Y W>

330     340     350
GGT CAA GGA ACC TCA GTC ACC GTC TCT TCA
CCA GTT CCT TGG AGT CAG TGG CAG AGA AGT
G Q G T S V T V S S>

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FIG. 4. Comparisons of framework regions of light chain of antibody hTNF40 and human group 1 consensus sequences

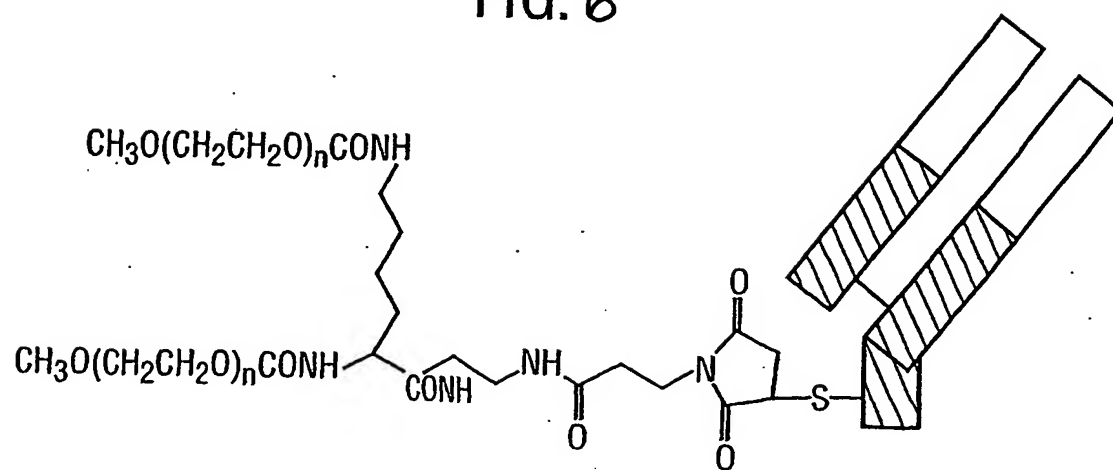
Hu group 1 consensus	: DIQMTQSPSSLSASVGDRVTTC (SEQ ID NO: 83)
hTNF40	: DIYMTQSQKFMSTSVGDRVSVTC (SEQ ID NO: 84)
Hu Group 1 consensus	: WYQQKPGKAPKLLIY (SEQ ID NO: 85)
hTNF40	: WYQQKPGQSPKALLIY (SEQ ID NO: 86)
Hu Group 1 consensus	: GVPSRFSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 87)
hTNF40	: GVPYRFSGSGTDFTLTISTVQSEDLA EY FC (SEQ ID NO: 88)
Hu Group 1 consensus	: FGQGTKVEIKR (SEQ ID NO: 89)
hTNF40	: FGAGTKLE L KR (SEQ ID NO: 90)

FIG. 5

Comparisons of framework regions of heavy chain of antibody hTNF40 and human group 1 and group 3 consensus sequences

Hu Group 1 consensus	: QVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO: 91)
hTNF40	: <u>Q</u> IQLVQSG <u>P</u> ELKKP <u>G</u> ETVKISCKASGY <u>V</u> FT (SEQ ID NO: 92)
Hu Group 1 consensus	: WVRQAPGQGLEWMG (SEQ ID NO: 93)
hTNF40	: WVKQAPGKAFKWMG (SEQ ID NO: 94)
Hu Group 1 consensus	: RVTITRDSTSTAYMELSSLRSEDTAVYYCAR (SEQ ID NO: 95)
hTNF40	: RFAFSLETSASTAFLOINN <u>L</u> KNEDTATYFCAR (SEQ ID NO: 96)
Hu Group 1 consensus	: WGQGTTLTVSS (SEQ ID NO: 97)
hTNF40	: WGQGT <u>T</u> TLTVSS (SEQ ID NO: 98)
Hu Group 3 consensus	: EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 106)
hTNF40	: <u>Q</u> IQLVQSG <u>P</u> ELKKP <u>G</u> ETVKISCKASGY <u>V</u> FT (SEQ ID NO: 92)
Hu Group 3 consensus	: WVRQAPGKGLEWVS (SEQ ID NO: 107)
hTNF40	: WVKQAPGKAFKWMG (SEQ ID NO: 94)
Hu Group 3 consensus	: RFTISRDN SKNTLYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 108)
hTNF40	: RFAFSLETSASTAFLOINN <u>L</u> KNEDTATYFCAR (SEQ ID NO: 96)
Hu Group 3 consensus	: WGQGTTLTVSS (SEQ ID NO: 109)
hTNF40	: WGQGT <u>T</u> TLTVSS (SEQ ID NO: 98)

FIG. 6



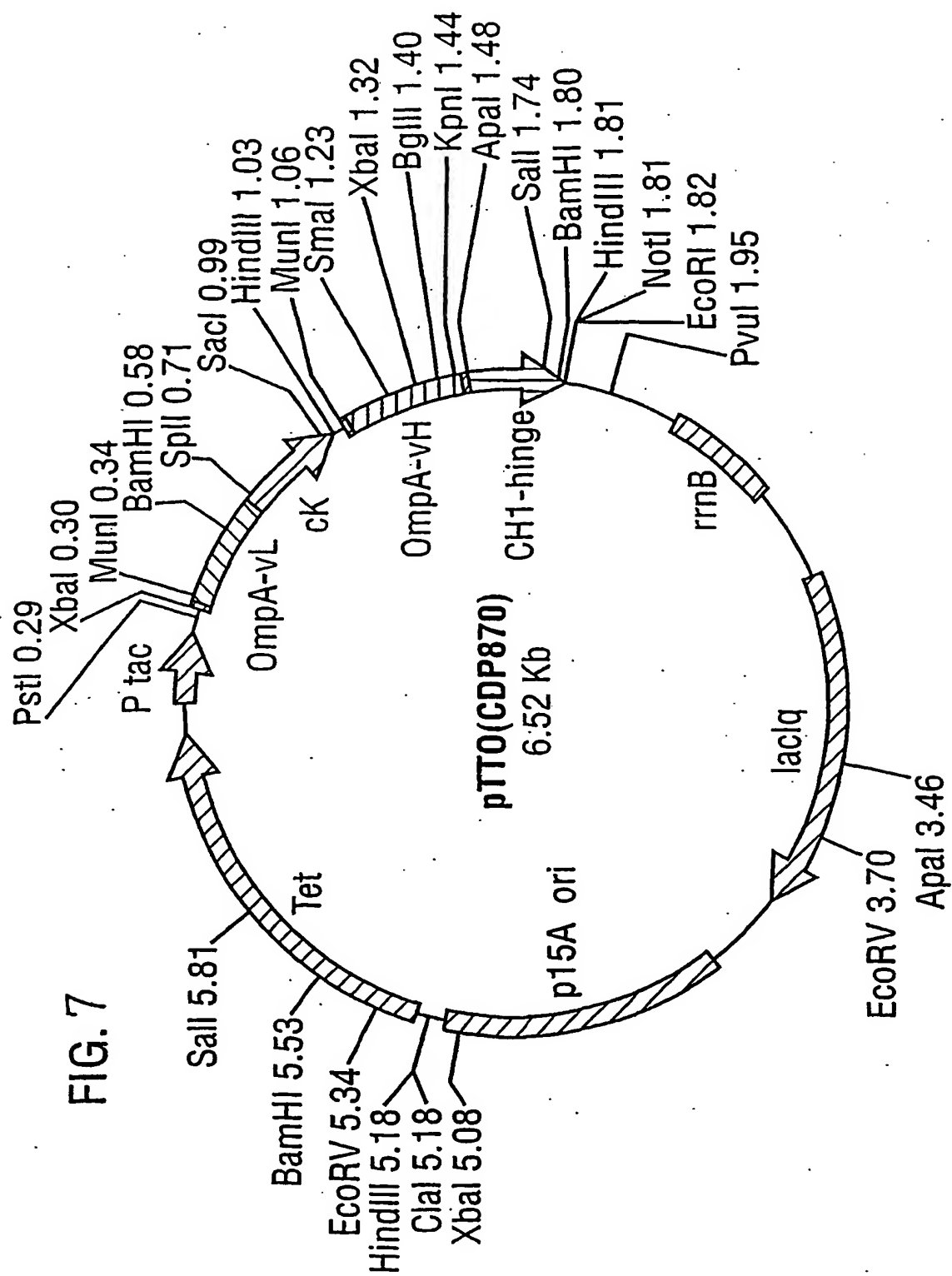


FIG. 7

FIG. 8

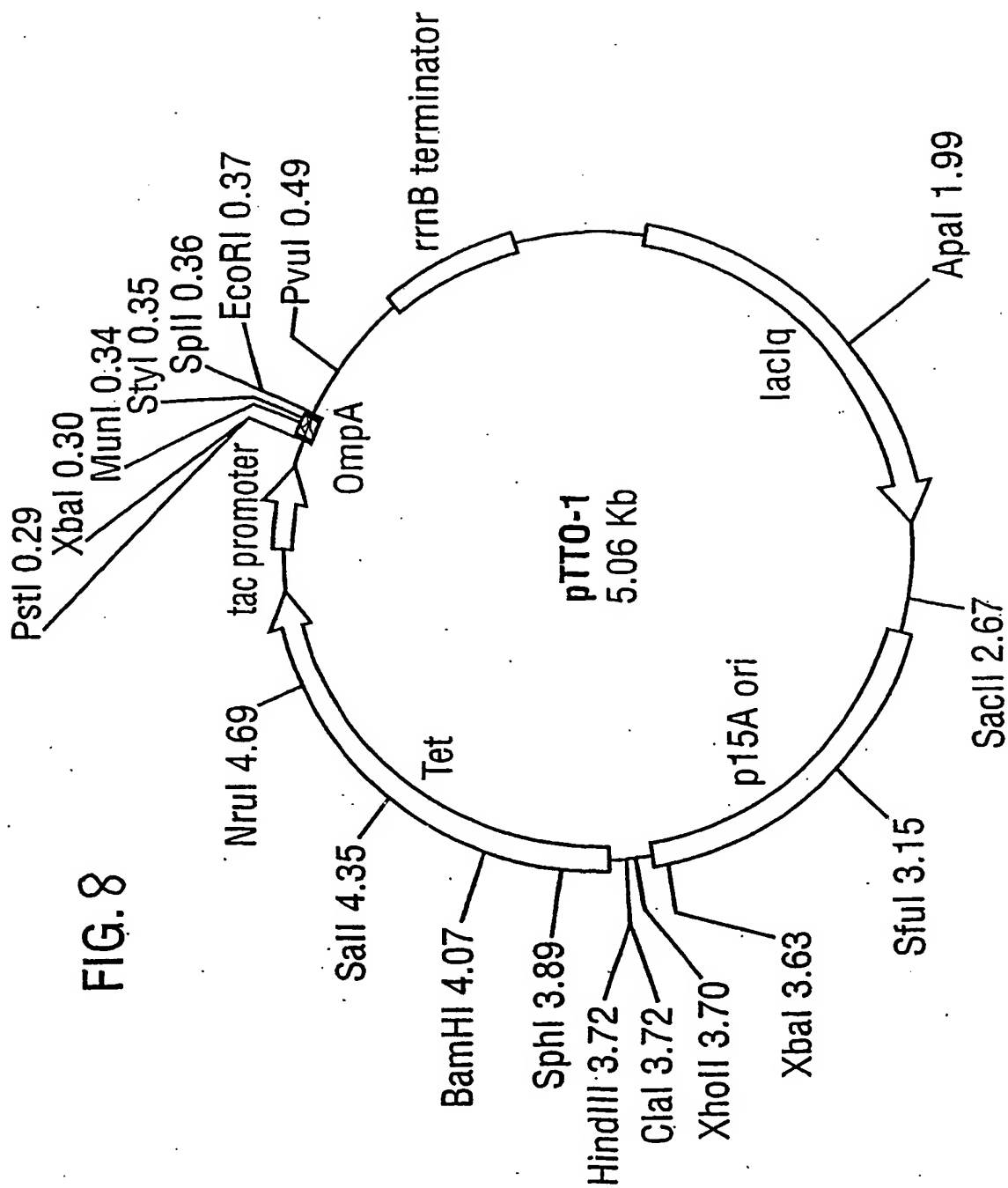


FIG. 9

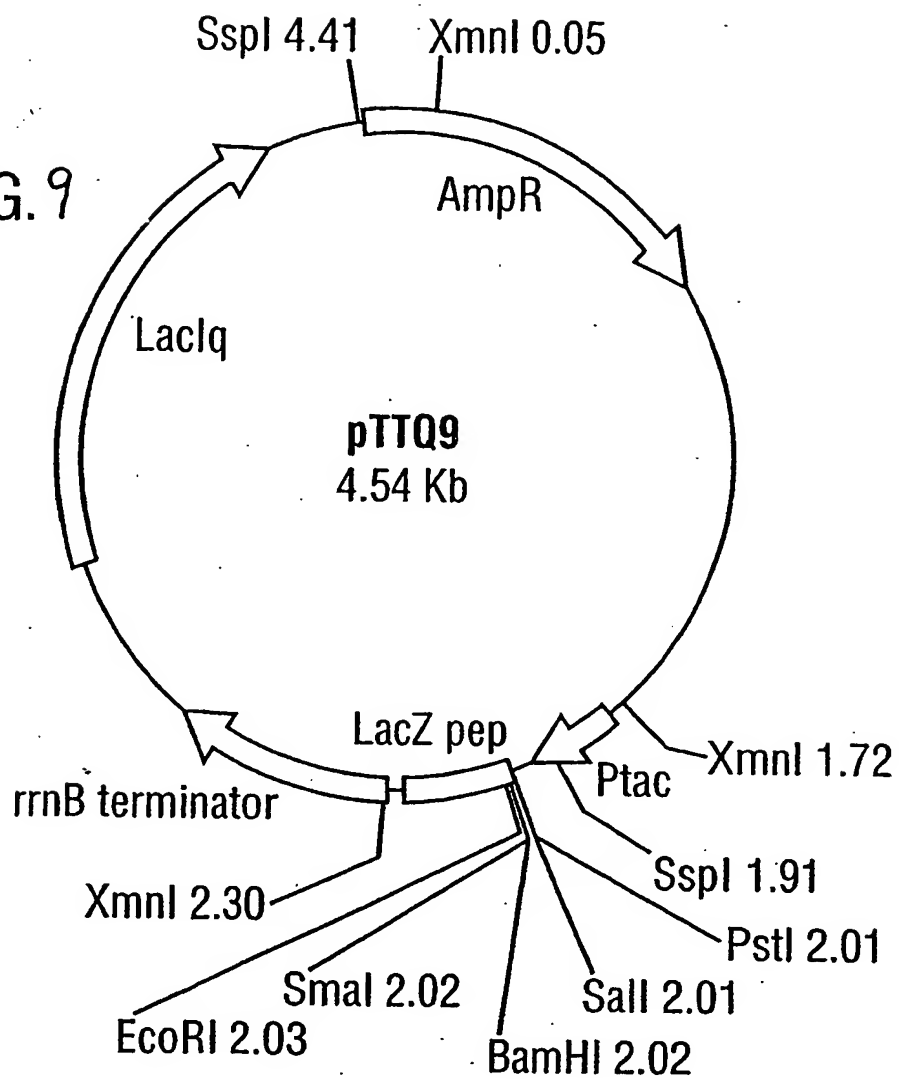
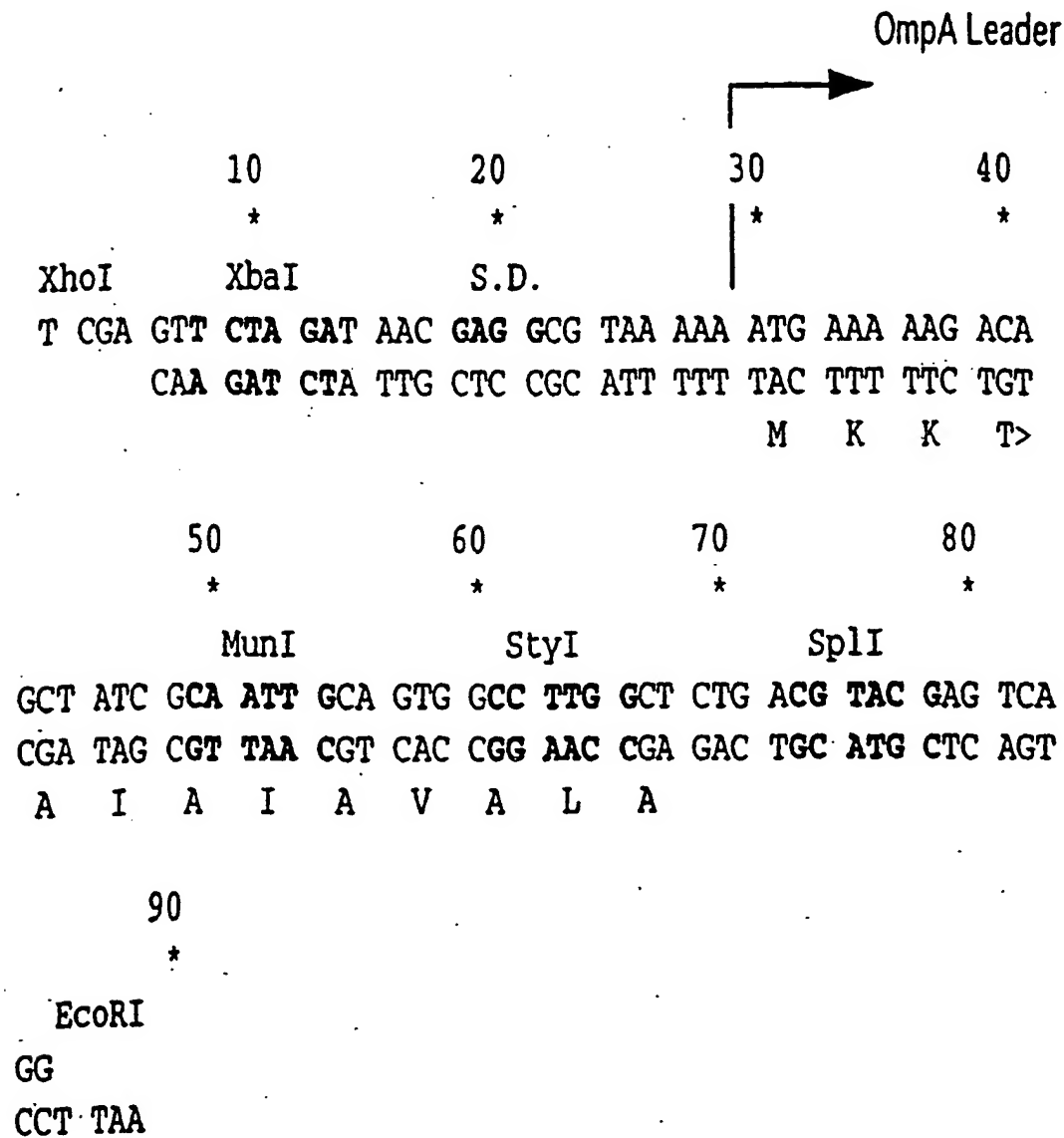


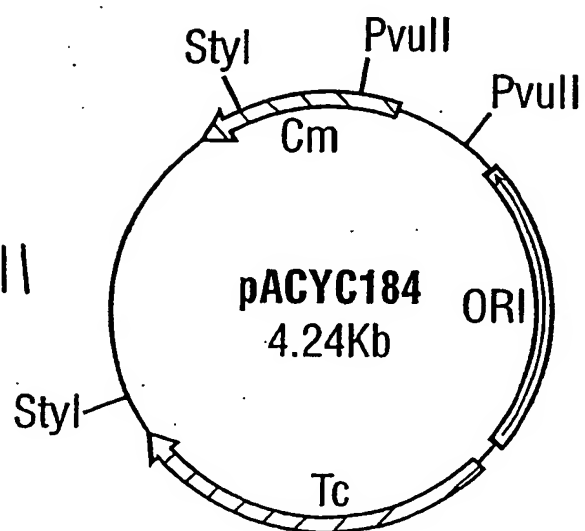
FIG. 10

Sequence of OmpA Oligonucleotide Adapter (SEQ ID NO: 101)



- Internal restriction sites are shown in bold
- The 5' XhoI cohesive end ligates into the Vector Sall site, blocking it
- S.D. represents the OmpA Shine Dalgarno sequence

FIG. 11



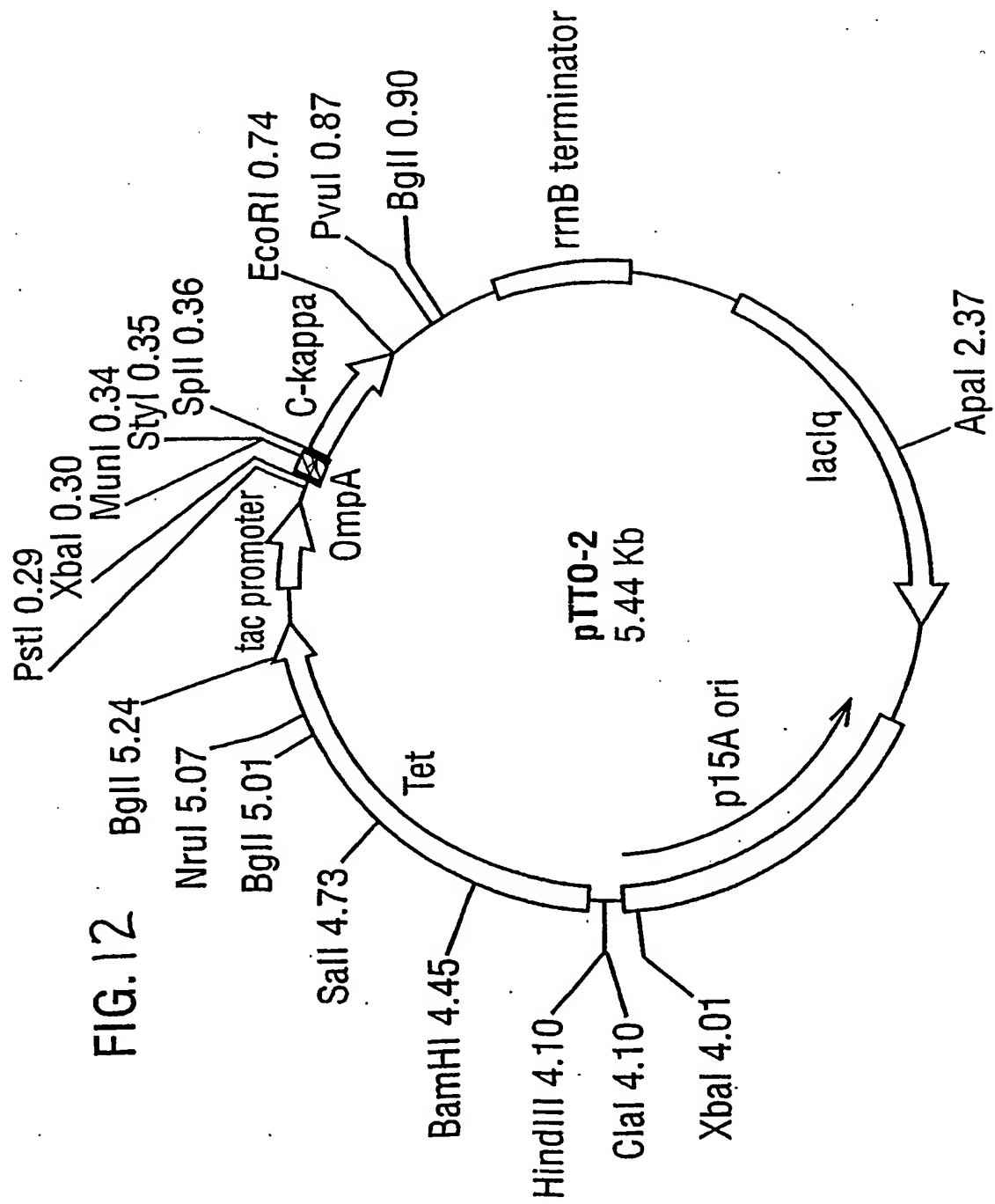


FIG. 13

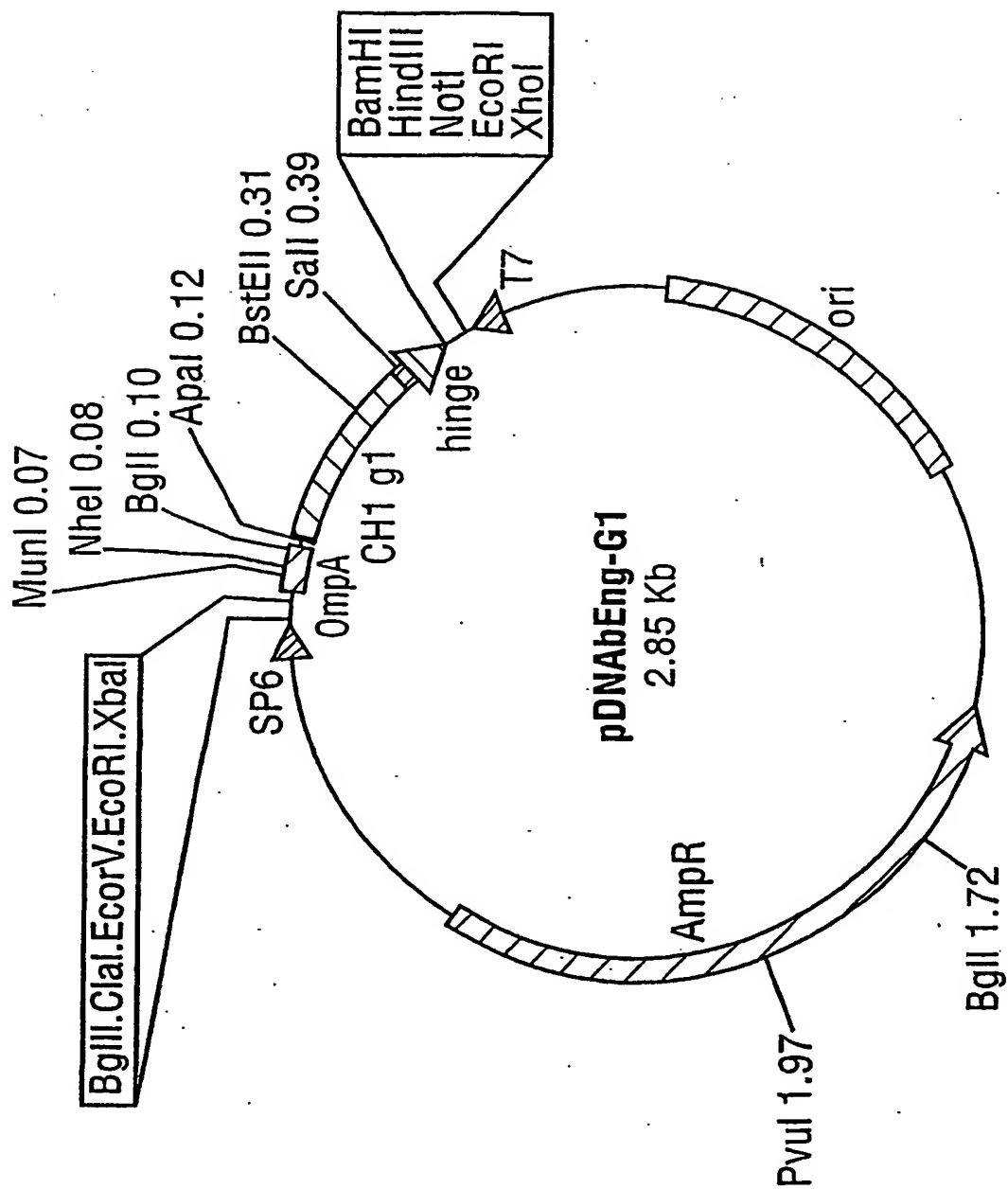


FIG.14 OLIGONUCLEOTIDE CASSETTES ENCODING DIFFERENT INTERGENIC SEQUENCES FOR E. Coli Fab' EXPRESSION

IGS CASSETTE-1; Intergenic space = -1

G, AGC, TCA, CCA, GTA, ACA, AAA, AGT, TTT, AAT, AGA, GGA, GAG, TGT, TAATG, AAG, AAG, ACT, GCT, ATA, GCA, ATT, G (SEQ ID No: 102)

S S P V T K S F N R G E C * M K K T A I A I

End of c-Kappa sequence ->

Start of OmpA sequence ->

IGS CASSETTE-2; Intergenic space = +1

G, AGC, TCA, CCA, GTA, ACA, AAA, AGT, TTT, AAT, AGA, GGG, GAG, TGT, TAA AATG, AAG, AAG, ACT, GCT, ATA, GCA, ATT, G (SEQ ID No: 103)

S S P V T K S F N R G E C * M K K T A I A I

IGS CASSETTE-3; Intergenic space = +13

G, AGC, TCA, CCA, GTA, ACA, AAA, AGC, TTT, AAT, AGA, GGA, GAG, TGT, TGA GGAGGAAAAAAATG, AAG, AAA, ACT, GCT, ATA, GCA, ATT, G (SEQ ID No: 104)

S S P V T K S F N R G E C * M K K T A I A I

IGS CASSETTE-4; Intergenic space = +13

G, AGC, TCA, CCA, GTA, ACA, AAA, AGT, TTT, AAT, AGA, GGA, GAG, TGT, TGA CGAGGATTATATAATG, AAG, AAA, ACT, GCT, ATA, GCA, ATT, G (SEQ ID No: 105)

S S P V T K S F N R G E C * M K K T A I A I

FIG.15 Grafted Vh Sequence of hTNF40.4 (SEQ ID NO: 11)

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10      20      30      40      50
GAG GTT CAG GTC GAG TCA GGA GGC GGT CTC GTG CAG CCT GGC GGA TCA CTG
CTC CAA GTC GAC CAG CTC AGT CCT CCG CCA GAG CAC GTC GGA CCG CCT AGT GAC
E V Q L V E S G G G L V Q P G G S L>

60      70      80      90      100
AGA TTG TCC TGT GCT GCA TCT GGT TAC GTC TTC ACA GAC TAT GGA ATG AAT TGG
TCT AAC AGG ACA CGA CGT AGA CCA ATG CAG AAG TGT CTG ATA CCT TAC TTA ACC
R L S C A A S G Y V F T D Y G M N W>

110     120     130     140     150     160
GTT AGA CAG GCC CCG GGA AAG GGC CTG GAA TGG ATG GGT TGG ATT AAT ACT TAC
CAA TCT GTC CGG GGC CCT TTC CCG GAC CTT ACC TAC CCA ACC TAA TTA TGA ATG
V R Q A P G K G L E W M G W I N T Y>

170     180     190     200     210
ATT GGA GAG CCT ATT TAT GCT GAC AGC GTC AAG GGC AGA TTC ACG TTC TCT CTA
TAA CCT CTC GGA TAA ATA CGA CTG TCG CAG TTC CCG TCT AAG TGC AAG AGA GAT
I G E P I Y A D S V K G R F T F S L>

220     230     240     250     260     270
GAC ACA TCC AAG TCA ACA GCA TAC CTC CAA ATG AAT AGC CTG AGA GCA GAG GAC
CTG TGT AGG TTC AGT TGT CGT ATG GAG GTT TAC TTA TCG GAC TCT CGT CTC CTG
D T S K S T A Y L Q M N S L R A E D>

280     290     300     310     320
ACC GCA GTG TAC TAT TGT GCT AGA GGA TAC AGA TCT TAT GCC ATG GAC TAC TGG
TGG CGT CAC ATG ATA ACA CGA TCT CCT ATG TCT AGA ATA CGG TAC CTG ATG ACC
T A V Y Y C A R G Y R S Y A M D Y W>

330     340     350
GGC CAG GGT ACC CTA GTC ACA GTC TCC TCA
CCG GTC CCA TGG GAT CAG TGT CAG AGG AGT
G Q G T L V T V S S>

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Figure 16

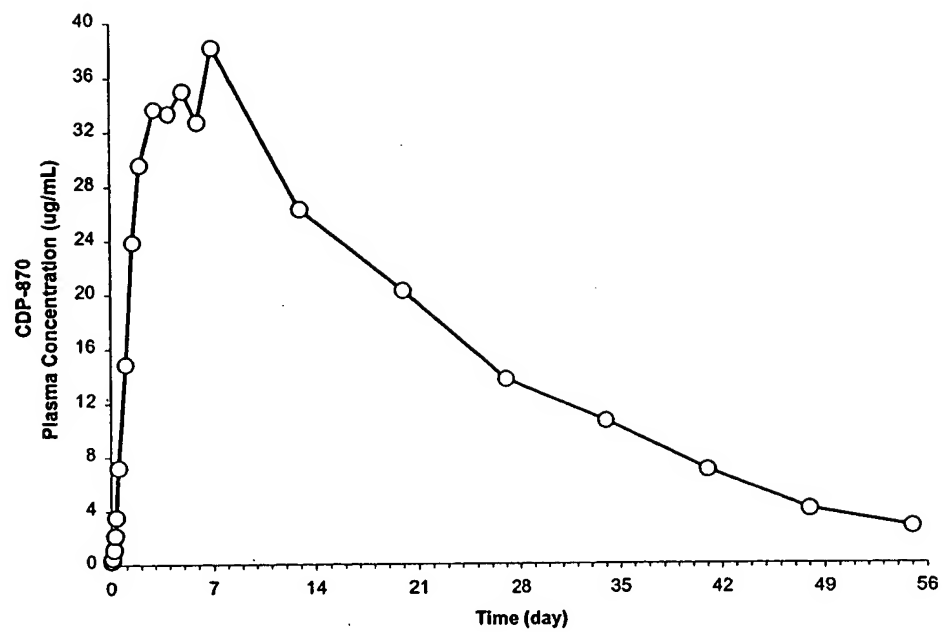


Figure 17

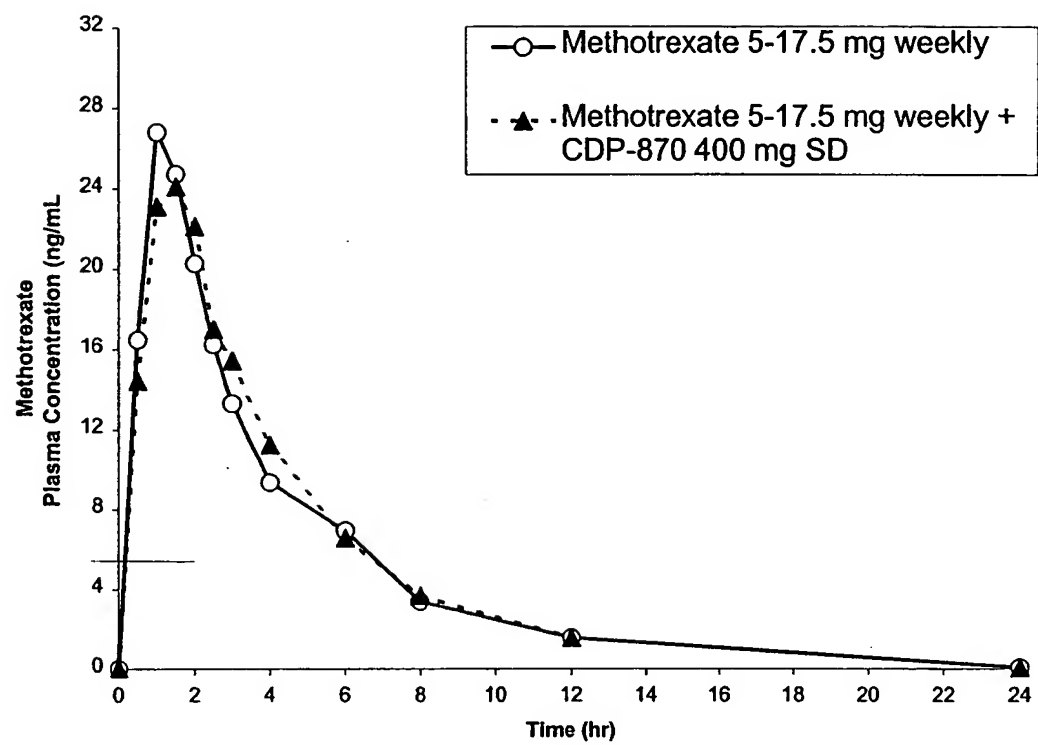


FIG. 18 CDP870 Heavy Chain mature protein sequence (SEQ ID NO: 115)

EVQLVESGGGLVQPGGSLRLSCAASGYVFTDYGMNWVRQAPGKGLEWMGWINTYIGE
PIYADSVKGRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCARGYRSYAMDYWGOGTLVTSSAS
TKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLS
VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCAA*

FIG. 19 CDP870 Light Chain mature protein sequence (SEQ ID No: 113)

DIQMTQSPSSLSASVGDRVTITCKASONVGTNVAWYQOKPGKAPKALIYSASFLYSGVP
YRFSGSGSGTDFLTITSSLOPEDFATYYCQYNIYPLTFGOGTKVEIKRTVAAPSVFIFPPSDEQLK
SGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHK
VYACEVTHQGLSPVTKSFNRGEC*

FIG. 20
(SEQ ID NOS: 116 – 117)

CDP870 nucleic acid sequences (shown as sense and anti-sense strands):

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      10      20      30      40      50
ATG AAA AAG ACA GCT ATC GCA ATT GCA GTG GCC TTG GCT GGT TTC GCT ACC GTA
TAC TTT TTC TGT CGA TAG CGT TAA CGT CAC CGG AAC CGA CCA AAG CGA TGG CAT

      60      70      80      90     100
GCG CAA GCT GAC ATT CAA ATG ACC CAG AGC CCA TCC AGC CTG AGC GCA TCT GTA
CGC GTT CGA CTG TAA GTT TAC TGG GTC TCG GGT AGG TCG GAC TCG CGT AGA CAT

110      120      130      140      150      160
GGA GAC CGG GTC ACC ATC ACT TGT AAA GCC AGT CAG AAC GTA GGT ACT AAC GTA
CCT CTG GCC CAG TGG TAG TGA ACA TTT CGG TCA GTC TTG CAT CCA TGA TTG CAT

      170      180      190      200      210
GCC TGG TAT CAG CAA AAA CCA GGT AAA GCC CCA AAA GCC CTC ATC TAC AGT GCC
CGG ACC ATA GTC GTT TTT GGT CCA TTT CGG GGT TTT CGG GAG TAG ATG TCA CGG

      220      230      240      250      260      270
TCT TTC CTC TAT AGT GGT GTA CCA TAC AGG TTC AGC GGA TCC GGT AGT GGT ACT
AGA AAG GAG ATA TCA CCA CAT GGT ATG TCC AAG TCG CCT AGG CCA TCA CCA TGA

      280      290      300      310      320
GAT TTC ACC CTC ACG ATC AGT AGC CTC CAG CCA GAA GAT TTC GCC ACT TAT TAC
CTA AAG TGG GAG TGC TAG TCA TCG GAG GTC GGT CTT CTA AAG CGG TGA ATA ATG

      330      340      350      360      370
TGT CAA CAG TAT AAC ATC TAC CCA CTC ACA TTC GGT CAG GGT ACT AAA GTA GAA
ACA GTT GTC ATA TTG TAG ATG GGT GAG TGT AAG CCA GTC CCA TGA TTT CAT CTT

380      390      400      410      420      430
ATC AAA CGT ACG GTA GCG GCC CCA TCT GTC TTC ATC TTC CCG CCA TCT GAT GAG
TAG TTT GCA TGC CAT CGC CGG GGT AGA CAG AAG TAG AAG GGC GGT AGA CTA CTC

      440      450      460      470      480
CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC TTC TAT CCC
GTC AAC TTT AGA CCT TGA CGG AGA CAA CAC ACG GAC GAC TTA TTG AAG ATA GGG

      490      500      510      520      530      540
AGA GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC
TCT CTC CGG TTT CAT GTC ACC TTC CAC CTA TTG CGG GAG GTT AGC CCA TTG AGG

      550      560      570      580      590
CAG GAG AGT GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC AGC CTC AGC AGC
GTC CTC TCA CAG TGT CTC GTC CTG TCG TTC CTG TCG TGG ATG TCG GAG TCG TCG
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FIG. 20 (cont'd)
(SEQ ID NOS: 116 – 117)

CDP870 nucleic acid sequences (shown as sense and anti-sense strands):

600	610	620	630	640	
ACC CTG ACG CTG AGC AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA					
TGG GAC TGC GAC TCG TTT CGT CTG ATG CTC TTT GTG TTT CAG ATG CGG ACG CTT					
650	660	670	680	690	700
GTC ACC CAT CAG GGC CTG AGC TCA CCA GTA ACA AAA AGC TTT AAT AGA GGA GAG					
CAG TGG GTA GTC CCG GAC TCG AGT GGT CAT TGT TTT TCG AAA TTA TCT CCT CTC					
710	720	730	740	750	
TGT TGA GG AGGAAAAAAAA A ATG AAG AAA ACT GCT ATA GCA ATT GCA GTG GCG CTA					
ACA ACT CC TCCTTTTTTT T TAC TTC TTT TGA CGA TAT CGT TAA CGT CAC CGC GAT					
760	770	780	790	800	810
GCT GGT TTC GCC ACC GTG GCG CAA GCT GAG GTT CAG CTG GTC GAG TCA GGA GGC					
CGA CCA AAG CGG TGG CAC CGC GTT CGA CTC CAA GTC GAC CAG CTC AGT CCT CCG					
820	830	840	850	860	
GGT CTC GTG CAG CCT GGC GGA TCA CTG AGA TTG TCC TGT GCT GCA TCT GGT TAC					
CCA GAG CAC GTC GGA CCG CCT AGT GAC TCT AAC AGG ACA CGA CGT AGA CCA ATG					
870	880	890	900	910	
GTC TTC ACA GAC TAT GGA ATG AAT TGG GTT AGA CAG GCC CCG GGA AAG GGC CTG					
CAG AAG TGT CTG ATA CCT TAC TTA ACC CAA TCT GTC CGG GGC CCT TTC CCG GAC					
920	930	940	950	960	970
GAA TGG ATG GGT TGG ATT AAT ACT TAC ATT GGA GAG CCT ATT TAT GCT GAC AGC					
CTT ACC TAC CCA ACC TAA TTA TGA ATG TAA CCT CTC GGA TAA ATA CGA CTG TCG					
980	990	1000	1010	1020	
GTC AAG GGC AGA TTC ACG TTC TCT CTA GAC ACA TCC AAG TCA ACA GCA TAC CTC					
CAG TTC CCG TCT AAG TGC AAG AGA GAT CTG TGT AGG TTC AGT TGT CGT ATG GAG					
1030	1040	1050	1060	1070	1080
CAA ATG AAT AGC CTG AGA GCA GAG GAC ACC GCA GTG TAC TAT TGT GCT AGA GGA					
GTT TAC TTA TCG GAC TCT CGT CTC CTG TGG CGT CAC ATG ATA ACA CGA TCT CCT					
1090	1100	1110	1120	1130	
TAC AGA TCT TAT GCC ATG GAC TAC TGG GGC CAG GGT ACC CTA GTC ACA GTC TCC					
ATG TCT AGA ATA CGG TAC CTG ATG ACC CCG GTC CCA TGG GAT CAG TGT CAG AGG					
1140	1150	1160	1170	1180	
TCA GCT TCC ACC AAG GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC					
AGT CGA AGG TGG TTC CCG GGT AGC CAG AAG GGG GAC CGT GGG AGG AGG TTC TCG					

FIG. 20 (cont'd)
(SEQ ID NOS: 116 – 117)

CDP870 nucleic acid sequences (shown as sense and anti-sense strands):

```
1190      1200      1210      1220      1230      1240
  ACC TCT GGG GGC ACA GCG GCC CTG GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA
  TGG AGA CCC CCG TGT CGC CGG GAC CCG ACG GAC CAG TTC CTG ATG AAG GGG CTT

      1250      1260      1270      1280      1290
  CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC
  GGC CAC TGC CAC AGC ACC TTG AGT CCG CGG GAC TGG TCG CCG CAC GTG TGG AAG

1300      1310      1320      1330      1340      1350
  CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG
  GGC CGA CAG GAT GTC AGG AGT CCT GAG ATG AGG GAG TCG TCG CAC CAC TGG CAC

      1360      1370      1380      1390      1400
  CCC TCC AGC AGC TTG GGC ACC CAG ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC
  GGG AGG TCG TCG AAC CCG TGG GTC TGG ATG TAG ACG TTG CAC TTA GTG TTC GGG

      1410      1420      1430      1440      1450
  AGC AAC ACC AAG GTC GAC AAG AAA GTT GAG CCC AAA TCT TGT GAC AAA ACT CAC
  TCG TTG TGG TTC CAG CTG TTC TTT CAA CTC GGG TTT AGA ACA CTG TTT TGA GTG

1460      1470
  ACA TGC GCC GCG TGA TGA
  TGT ACG CGG CGC ACT ACT
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